

## ENHANCED TRANSPORT USING MEMBRANE DISRUPTIVE AGENTS

### Abstract of the Invention

5           Compositions and methods for transport or release of therapeutic  
and diagnostic agents or metabolites or other analytes from cells, compartments  
within cells, or through cell layers or barriers are described. The compositions  
include a membrane barrier transport enhancing agent and are usually  
administered in combination with an enhancer and/or exposure to stimuli to  
10   effect disruption or altered permeability, transport or release. In a preferred  
embodiment, the compositions include compounds which disrupt endosomal  
membranes in response to the low pH in the endosomes but which are relatively  
inactive toward cell membranes (at physiologic pH, but can become active  
toward cell membranes if the environment is acidified below ca. pH 6.8),  
15   coupled directly or indirectly to a therapeutic or diagnostic agent. Other  
disruptive agents can also be used, responsive to stimuli and/or enhancers other  
than pH, such as light, electrical stimuli, electromagnetic stimuli, ultrasound,  
temperature, or combinations thereof. The compounds can be coupled by ionic,  
covalent or H bonds to an agent to be delivered or to a ligand which forms a  
20   complex with the agent to be delivered. Agents to be delivered can be  
therapeutic and/or diagnostic agents. Treatments which enhance delivery such  
as ultrasound, iontophoresis, and/or electrophoresis can also be used with the  
disrupting agents.